NEBRASKA HEALTH AND HUMAN SERVICES SYSTEM

ACT SHEET FOR POSITIVE NEWBORN SCREENING RESULT FOR HEMOGLOBIN BART'S (FA+Bart's, FAV+Bart's, FVA+Bart's)

Disease Category: Hemoglobinopathy

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact the family to inform them of the screening result and offer education and counseling.
- Order confirmatory testing by HPLC/hemoglobin electorphoresis. Collect 0.5ml EDTA (purple top) whole blood from the infant to be tested.
- Encourage family members to seek testing for thalassemia and hemoglobin variants followed by genetic counseling.
- Following initial confirmatory testing, referral to pediatric hematologist may be indicated for definitive diagnosis.
- Report findings to state newborn screening program.

Pediatric specialists in hemoglobinopathies are available at Children's Hospital (402) 955-3950 and Nebraska Medical Center (402) 559-7257.

Meaning of the Screening result: Alpha thalassemia – any of 4 types. Alpha thalassemia 2 silent carrier is a result of a single gene deletion, which will have no clinical significance. Alpha thalassemia trait results from loss of two genes and causes a mild microcytic anemia. Hemoglobin H disease is a moderately severe form of thalassemia resulting from the loss of 3 genes.

Hydrops fetalis results from the 4-gene deletion which would be unlikely to be detected on a newborn screen since newborns do not survive more than a few hours.

Confirmation of Diagnosis: Hemoglobin electorphoresis to separate those with trait from silent carrier.

Additional Information:

- Acute and Chronic Complications - www.tdh.state.tx.us/newborn/sc_guide.htm
- Grady Comprehensive Sickle Cell Center Web Site – www.scinfo.org
- Management and Therapy of Sickle Cell Disease - www.nhlbi.nih.gov/health/prof/blood/sickle/index.htm
- Sickle Cell Disease Association - www.sicklecelldisease.org
- Sickle Cell Disease in Children and Adolescents: Diagnosis, Guidelines for Comprehensive Care and Protocols for Management of Acute and Chronic Complications www.tdh.state.tx.us/newborns/sc_guide.htm

BACKGROUND:

The alpha thalassemias result from the loss of alpha globin genes. There are normally four genes for alpha globin production so that the loss of one to four genes is possible.

The lack of one gene causes alpha thalassemia 2 (silent carrier) with no clinically detectable problems but may cause small amounts of hemoglobin Bart's to be present in newborn blood samples. Alpha thalassemia trait (Alpha thalassemia 1) results from loss of two genes and

causes a mild microcytic anemia, which may resemble iron deficiency anemia. The loss of three genes causes hemoglobin H diseases, which is a moderately severe form of thalassemia. The lack of all four genes causes hydrops fetalis and is usually fatal in utero.

In general, only the loss of one or two genes is seen in African Americans. Individuals from Southeast Asia and the Mediterranean may have all four types of alpha thalassemia.

The percentage of hemoglobin Bart's in the blood sample may indicate the number of alpha genes that have been lost. However, the percentage of hemoglobin Bart's is not directly measurable with the current methodology used by the newborn screening laboratory. Only the presence of Bart's hemoglobin in relation to fetal and adult hemoglobin, and variants S, C, D and E can be detected.

RECOMMENDED WORK UP:
In addition to the standard newborn hemoglobinopathy confirmation (hemoglobin electrophoresis), to separate those patients with alpha thalassemia silent carrier from the patients with alpha thalassemia trait, we recommend that these babies have the following labs drawn at their 6 month well baby check: CBC with retic count, ferritin, and a hemoglobin electropheresis. The patient with alpha thalassemia silent carrier should have a normal CBC and retic, and a normal electrophoresis. A patient with alpha thalassemia trait will generally have a normal hemoglobin electrophoresis and retic, but microcytic red blood cells with an elevated red blood cell number. The hemoglobin in patients with alpha thalassemia trait may be slightly below normal to normal. The ferritin level reflects stored iron reserves. Many subtle hemoglobin defects like alpha thalassemia trait are not reliably diagnosed in the presence of iron deficiency. Documenting that the patient's iron level is normal improves the validity of the work up.

CLINICAL MANAGEMENT:
Individuals with alpha thalassemia trait may have a very mild anemia with microcytosis and no other clinical problems. This anemia however, may be confused with iron deficiency anemia. Parents of infants with diagnosed hemoglobin Bart's (alpha thalassemia trait), should be told it is inherited and that others in the family may have a similar disorder. They should be instructed to tell health professionals that their child has alpha thalassemia trait to avoid unnecessary tests or treatment with iron. These patients, like any child are capable of becoming iron deficient. Rather than relying on "trials of iron" or other empiric therapy, when iron deficiency is suspected in these children, it should be worked up and treated formally.

GENETIC COUNSELING:
Family studies may be indicated after confirmatory testing of the newborn, to detect the more serious forms of alpha thalassemia. Particularly in those children who have a southeast Asian heritage, or in multiracial children, family studies may be useful as these ethnic groups have an increased risk for the more serious forms of alpha thalassemia and documenting this risk status may be useful in genetic counseling or family planning.

If you have additional questions, please call Dr. James Harper of the pediatric hematology clinic at UNMC at (402) 559-7257. Other hematology specialists are available at (402) 955-3950 Dr. David Gnarra at Children's Hospital or (308) 762-2125 Dr. Howard Koch in Alliance.